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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,427	12/12/2001	Harshal P. Bhagwatwar	U 013528-7	2278

140 7590 03/27/2008

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
03/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/023,427	BHAGWATWAR ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-90,93,96,97 and 99-101* is/are pending in the application.

4a) Of the above claim(s) *100 and 101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-90,93,96,97 and 99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of IDS, amendment and remarks filed 12/18/07. Claims 72, 73, 76, 83, 85, 86, 88, 96 and 97 are amended; claims 98 and 102 are canceled. Therefore, claims 72-90, 93, 96, 97 and 99-101 are pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Matters addressed by applicant on pages 7 and 8 of the remarks:

A. Withdrawal of claims 100-102: The examiner agrees with applicant that the restriction requirement of 8/19/2003 was withdrawn in the office action of 12/2/2003 and claim 52 was rejected under 35 USC 112, first paragraph in view of the language of preventing. However, claims 100-102, with claim 102 canceled by the amendment of 12/28/07, differ from original claim 52 as shown below:

52. (Original) A method of preventing or treating a health disorder, disease or medical condition comprising administering a composition according to claim 1 to a patient in need thereof.

New claims 100 and 101 (102 canceled) presented with the RCE, now indicated as withdrawn are properly withdrawn from consideration because while prostate cancer and breast cancer are specific medical conditions of health disorder for reasons on record. The product in claim 1 used to practice claim 52 is not the product that is used to treat the specific disorders in claims 100 and 101

100. (Withdrawn) A method for treating prostate cancer comprising administering to a subject in need thereof the drug delivery according to claim 83 wherein the biologically active agent is leuprolide acetate.

101. (Withdrawn) A method for treating breast cancer comprising administering to a subject in need thereof the drug delivery according to claim 83 wherein the biologically active agent is paclitaxel.

B. References used in the art rejections:

Applicant has chosen to use: Jain et. al. "Controlled drug delivery from a novel injectable in situ formed biodegradable PLGA microsphere system," in Journal of Microencapsulation, 17 (3), 343-362 (2000) in the arguments instead of the dissertation of Jain. However, the rejection was made over the dissertation of Jain and rejections maintained over the dissertation and sections of the dissertation are used to support the rejection.

C. Applicant states that the other two journal articles were published later in December while the articles in the Journal of Microencapsulation was published in May of 2000 and preferred to use that in the arguments.

But:

Jain et al. ("Comparison of Various Injectable Protein-Loaded Biodegradable Poly(Lactide-co-glycolide) (PLGA) devices: In situ-Formed Implant Versus In-Situ-Formed Microspheres Versus Isolated Microspheres," in Pharmaceutical Development and Technology, 5(2), 201-207 (2000)) was published in April of 2000 and,

Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490) was published in Dec. 1 of 2000.

Both dates are earlier than the priority date of 12/18/2000 and thus, while the examiner responds to applicant's arguments using the Journal of Microencapsulation article, the examiner also maintains those rejections and refers to the references in the response to applicant's argument.

Claim Rejections - 35 USC § 112/New Matter

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 72-90, 93, 96, 97, 99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The requirement by the amended claim 72 that the delivery system consist of a), b) and c) excludes the biologically inactive agent from the composition. A composition that excludes biologically inactive agent was not envisioned at the time the original application was filed. See for example the abstract, paragraphs [0008],[0012], [0014], [0015] and [0016] where it is

specifically stated that the delivery device is for delivery of bioactive or bio-inactive agents. Applicant may overcome this rejection by deleting the new matter from the claims.

4. Claims 72-90, 93, 96, 97and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 72 b) requires the discontinuous phase to consist of polymer that is dissolved in water soluble organic solvent, but claim 72 c) requires that an agent be dispersed in the discontinuous phase. However, since the discontinuous phase consists of polymer, the discontinuous phase cannot then have biologically active agent. It is thus confusing how the discontinuous phase contains biologically active agent.

Claim 93 requires that the drug delivery device/system further contain biologically inactive agent and it is unclear how the delivery system of claim 72 that consists of a, b and c further contains biologically inactive agent.

Clarification is respectfully requested.

Claim 93 requires the composition of claim 72 to further contain biological agent and it is not clear how the composition or delivery system that already contains biologically active agent further contains biologically active agent.

Clarification is respectfully requested.

Claim 97 requires an aqueous medium and it is confusing how the claimed delivery system of claim 72, which is consists of a), b) and c) would contain an aqueous phase as required by dependent claim 97. Claim 97 as presented contradicts the concept of the claimed delivery system of claim 72.

Clarification is respectfully requested.

Claim 99 requires that the continuous phase further contain biologically active agent and this contradicts the requirement of claim 72 that the deliver device consist of a), b) and c).

Clarification is respectfully requested.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 72-79, 84, 87, 93 and 96-99 are rejected under 35 U.S.C. 102(b) as being anticipated by Jain ("controlled drug delivery from a novel injectable in situ formed biodegradable PLGA mocrosphere system," Dissertation, University of Rhode Island, 1998, abstract, cited in applicant's specification; full document submitted by applicant on 9/11/07).

Jain describes a delivery system that comprises polymer is organic solvent, polymer and emulsifier/surfactant in oil and drug; PEG meeting claim 76 is present; TWEEN meeting the requirements for surfactant/emulsifier in claims 72 and 98 is present (see abstract). Claims 77-79 is product by process claim and reads on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention.

The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the drug of Jain. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

7. Claims 72-79, 84, 87, 93 and 96-99 are rejected under 35 U.S.C. 102(a) as being anticipated by Jain et al. ("Comparison of Various Injectable Protein-Loaded Biodegradable Poly(Lactide-co-glycolide) (PLGA) devices: In situ-Formed Implant Versus In-Situ-Formed Microspheres Versus Isolated Microspheres," in Pharmaceutical Development and Technology, 5(2), 201-207 (2000)).

Jain describes a delivery system that comprises polymer is organic solvent, polymer and emulsifier/surfactant in oil and bovine heart cytochrome c; PEG meeting claim 76 is present; TWEEN meeting the requirements for surfactant/emulsifier in claims 72 and 98 is present (see abstract and pages 201-207). Claims 77-79 is product by process claim and reads on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention. The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the bovine heart cytochrome c of Jain. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

8. Claims 72-80, 82, 84, 87, 93 and 96-98 are rejected under 35 U.S.C. 102(a) as being anticipated by Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain describes composition comprising drugs such as peptides, vaccines, proteins and micromolecules (abstract); the oil phase I contains PLGA, triacetin (organic solvent for the PLGA), TWEEN-80, drug, PEG and oil phase II contains miglyol and SPAN 80; the two phases are mixed to form dispersions that upon administration to target site containing water form microspheres in situ (page 2483 and 2484). Claims 77-79 are product by process claims and read on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention. The vaccine of Jain meets claim 82. The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the drugs/vaccines/peptides/protein of Jain. The oily phase II containing miglyol 812, which is oil and Span 80, which is an emulsifier or surfactant is the continuous hydrophobic phase and the Span 80 is a sorbitan ester meeting claim 80. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

Response to Arguments

9. Applicant's arguments filed 12/28/07 have been fully considered but they are not persuasive.

10. Applicant argues: (Arguments specifically directed to the Jain, Dissertation)

a) *that Jain uses TWEEN 80 in the discontinuous phase*, but on page 73 at the second full paragraph, Jain puts Span 80 in miglyol, which is oil, and claim 72 a) dissolves emulsifier in the oily phase

b) *that Jain says that that in the absence of TWEEN 80, PLGA microglobules that poorly disperses in contact with water into agglomerated mass*, but, it is noted that page claim 72 a) does not exclude TWEEN as an emulsifier.

c) *that Jain's delivery system is different from the claimed delivery system because Jain does not disclose the use of vaccines for formulating in situ delivery system*. However, while applicant states the above about Jain, the applicant also admits that the claimed composition does not describe the actual use of vaccines but has provided enough description in the prior art delivery compositions and in this case also the claims have not used vaccines so that the argument regarding vaccine is moot.

d) *that triacetin is water immiscible*, but triacetin is water soluble/miscible as evidenced by claim 31 of Synosky et al. (US 5,436,013).

e) *that the droplet in claims 73, 77-79 and 84 are gelled*. Similarly, the droplet of Jain is gelled because Jain describes the presence of surfactants such as sorbitan fatty esters in the continuous oily phase (page 20, second and third full paragraphs extending into page 21) and on page 73 at the second full paragraph, SPAN 80 is dissolved in the continuous phase provided by miglyol, a triglyceride.

f) *that Jain adds the drug to the discontinuous phase*, but this is consistent with claim 72 c).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 81 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. Jain uses Span 80, a sorbitan monooleate is a sorbitan ester. Regarding claim 81, which limits the sorbitan ester to sorbitan monopalmitate and sorbitan monostearate, it is known that sorbitan monooleate is a sorbitan ester just as the claimed sorbitan monopalmitate and sorbitan monostearate and one sorbitan ester can be used in place of the other with the expectation of obtaining the same degree of emulsification of the oily phase.

The difference between the prior art and claim 85 is in the concentration of the polymer in the organic phase. The concentration of the polymer in the organic solvent is at a broad

concentration of between 1 and 90% so that an artisan is able to use appropriate amount of the polymer in the organic solvent that would provide desired release of the drug. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the delivery system of Jain with using a concentration of polymer in the organic solvent that would provide the desired release.

Response to Arguments

14. Applicant's arguments filed 12/28/07 have been fully considered but they are not persuasive.

15. Applicant argues"

g) *that with regard to claim 81, Jain teaches away from the invention because, the composition of Jain is not gelled while the instant composition is gelled because the role of SPAN in the instant composition is to gel the continuous oil phase*. However, the continuous oil phase of Jain provided by the triglyceride miglyol contains SPAN as shown on page 73, first full paragraph.

16. h) *that with regard to claim 85, Jain teaches away from the claim because the Journal of Microencapsulation article, vol. 17, issue 3, pp. 343-362 (2000) by Jain provides a critical ratio of PLGA/triacetin at 0.05-0.22 while the polymer concentration in the invention ranges from 1-90%w, preferably from 5-70% w/w, and more preferably from 10-60% w/w at paragraph [0055]*. In response to the preceding argument, it is noted that it was the dissertation of Jan that was used in the rejection and on page 73 of the dissertation, no specific amount of the PLGA and triacetin was used. Secondly, claim 85 recites a broad range of 1-90% w/w polymer in the organic solvent and 10-60% w/w and 56-70% w/w are limitations from the specification.

Thirdly, Jain in the journal of microencapsulation article at page 351 at the first full paragraph specifically talks about a ratio of PLGA/triacetin and the amounts referred/cited by applicant is ratio and not percent so that a comparison cannot really be made between the ratio and the percent. However, when the % recited in claim 85 is converted to ratio of PLGA/triacetin of 1/99 – 90/10 == 0.01 to 9, then the ratio specifically noted as critical at 0.05-0.22 would touch points within the recited range of 0.01-9. Therefore, Jain in the journal article does not teach away form claim 85. Therefore claims 81 and 85 are rendered obvious according to the rejections above.

17. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. The difference between the prior art and claim 86 is in the concentration of the emulsifier with respect to the polymer and the organic solvent. The concentration of the emulsifier relative to the organic solvent and the polymer is at a broad concentration of between 0.01 and 50% so that an artisan is able to use appropriate amount of the emulsifier in the organic solvent and the polymer that would provide desired emulsification of the oily phases. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the delivery system of Jain with using a concentration of emulsifiers relative to the organic solvent and the polymer that would provide the desired emulsification of the phases.

Response to Arguments

18. Applicant's arguments filed 12/28/07 have been fully considered but they are not persuasive.

i) *Applicant argues that triacetin is water immiscible*, but as stated above in paragraph 10 c), triacetin is water soluble/miscible as evidenced by claim 31 of Synosky et al. (US 5,436,013). Using triacetin, a water soluble solvent does not represent obvious to trying water immiscible solvent when water miscible solvent is called for by the claims. Claim 86 deals with continuous phase and not with the discontinuous phase. The difference between the prior art and the claim is in the amounts and taking the teaching of the reference, one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success that using appropriate concentrations of the continuous phase with the discontinuous phase would provide the desired emulsification of the phases.

19. Claims 88-90 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. The difference between Jain and claims 88-90 is the Jain, while disclosing formation of microparticles upon contact of the oily composition with water, does not specifically disclose the particle sizes. However, since the particles are formed by the same process and from the same composition, it would flow that the particles would have the same particle distribution. However, in the alternate, the particles size or the Jain reference would

obviously fall within the claimed particle sizes since the particles formed in the claims and the prior art are formed from the same composition and the same process of contacting the composition with an aqueous environment.

Response to Arguments

20. Applicant's arguments filed 12/28/07 have been fully considered but they are not persuasive.

21. Applicant argues:

22. j) *that the composition of Jain is not gelled and that in the absence of TWEEN PLGA microglobules are poorly dispersed and that in the instant case TWEENs are not used as emulsifiers.* In response to this argument, it is clear that claim 72 a) is open, the emulsifier is open to any emulsifiers, the emulsifier is dissolved in an oily phase so that the presence of TWEEN in the oily discontinuous phase does not go against claim 72 a) and claim 72 as a whole. There is thus no issue here about obvious to try. Therefore, Jain does not teach away from the invention. Claims 88-90 remain rejected according to the rejections on record and as reiterated herein.

No claim is allowed.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Blessing M. Fubara/
Examiner, Art Unit 1618